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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MOORE, WILLIAM W.	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 09/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/624,945	YEH ET AL.	
	Examiner	Art Unit	
	William W. Moore	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-63* is/are pending in the application.

4a) Of the above claim(s) *51 and 53* is/are withdrawn from consideration.

5)☒ Claim(s) *63* is/are allowed.

6)☒ Claim(s) *45-50,52 and 55-62* is/are rejected.

7)☒ Claim(s) *54* is/are objected to.

8)☒ Claim(s) *51 and 53* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20030915*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election

Applicant's election **without** traverse in the Response filed 12 July 2006 of the invention of Group I, claims comprising claims 45-50 drawn in part to, and claims 52 and 55-63 drawn particularly to, a protease comprising all or part of a SENP1 protease having the amino acid sequence set forth in SEQ ID NO:2, is acknowledged. Applicant does not expressly traverse the requirement for restriction but suggests at pages of the Response that claims 51 and 53 describing proteases of Groups II and III may be examined together with the protease of the invention of Group I because "claims 45 and 54 are proper linking claims with respect to the claims in Groups II and III" and that, "should the proper linking claims [45 and 54] be allowed, claims 51 and 53 should be examined under MPEP § 809 as to nonelected inventions." Applicant does not argue that the search burdens for inventions of Groups II and III are the same search burden required for examining the elected invention of Group I.

The requirement is still deemed proper and is therefore made FINAL because, as noted at page 3 of the communication mailed 12 June 2006, the invention of Group 1 is an invention unrelated to inventions of Groups II and III where "each protease is an independent chemical entity having a structure distinct from those of the other proteases, requiring separate searches in commercial and USPTO amino acid sequence databases and in the publications of the prior art . . . where . . . each search is a separate burden on the resources of the USPTO." Claims 51 and 53 are therefore withdrawn from further consideration, and the subject matters of claims 45-50, 52, and 55 are examined to the extent to which they describe a protease comprising all or part of a SENP1 protease having the amino acid sequence of SEQ ID NO:2. Election was made **without** traverse in the Response filed on 12 July 2006.

Information Disclosure Statement

Applicant's Information Disclosure Statement, Paper No. 8 filed March 11, 2002, is hereby acknowledged and the documents submitted therewith are made of record on the PTO Forms 1449 supplied by Applicant that accompany this communication.

Objection to the Specification for Introduction of New Matter

The amendment filed 22 July 2003, and recapitulated in the Response filed 12 July 2006, is objected to under 35 U.S.C. § 132(a) because it introduces new matter into the disclosure. 35 U.S.C. § 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure of the parent application and the original claims 1-44 is as follows:

1) The recitation in claim 45 of the nonapeptide sequence "PIH$^{L}/_{R}$XVHW" which is not present anywhere in the specification or claims of Applicant's provisional application priority document serial No. 60/146,774, in the specification or claims of the parent utility application serial No. 09/628,966, or in the claims 1-44 filed with the instant specification and that are the claims 1-44 of the parent application serial No. 09/628,966.

2) The recitations in claims 52, 61, and 62, of specific amino terminal regions for an isolated sentrin-specific protease constitute new matter because the specification does not define, state, disclose, or suggest any specific amino-proximal boundary of a carboxyl-terminal portion of SEQ ID NO:2. Applicant is required to cancel the new matter in the reply to this Office Action.

Objection to the Specification for Lack of Sequence Rules Compliance

The disclosure is objected to due for lack of compliance with 37 CFR § 1.821 which compliance required in response to this Office action. Claim 45 lacks a designation describing the subject matter of the recited nonapeptide according to requirements of 37 CFR § 1.821 for a Sequence Disclosure and the Sequence Listing lacks a sequence

entry and sequence identifier for the recited nonapeptide in the format, "**SEQ ID NO:n**", where "n" is an integer corresponding to the Sequence Disclosure. Should Applicant establish a basis for an adequate written disclosure of the nonapeptide supporting its recitation in a claim Applicant must, in response to this communication, file a revised Sequence disclosure in printed and computer-readable forms including the nonapeptide and an appropriate sequence identifier as well as a Statement that the contents of the printed and computer-readable forms are the same. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 45-50, 52, and 55-62 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claim 45-54, 61, and 62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. For the reasons set forth above in the objection to the specification for introduction of new matter, claims 45-54, 61, and 62 contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection does not affect either claim 54, the elected subject matter of which describes the sentrin-specific protease that comprises the amino acid sequence set forth in SEQ ID NO:2, or claim 63, which is drawn specifically to a sentrin-specific protease that comprises the amino acid sequence set forth in SEQ ID NO:2. It is noted

that amending claim 54 to remove the non-elected subject matter it describes would render claims 54 and 63 substantial duplicates, one of the other.

Claims 45-50 and 55-60 are separately rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed because the specification does not teach those particular features of a sentrin-specific protease that permit it to recognize and bind to a sentrinized protein and subsequently cleave a sentrin-1 or sentrin-2 peptide from the sentrinized protein. The specification fails to exemplify or describe the preparation or discovery of the subject matters of products of claims 45-50 and 55-60 to the extent these products differ, as indicated at page 5, lines 1-3, and pages 24 and 25 of the specification, from the structure of a SENP1 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2. Claim 54 describes a nonapeptide region common to six sentrin-specific proteases as depicted in Table 5 but this constitutes a very small fraction of such proteases. Even the limitations of claim 50, which describes in part Applicant's elected subject matter, and of claim 60, permit molecules described by the claims to differ from the amino acid sequence of SEQ ID NO:2 at as much as 70% in claims 50 and 60 from the amino acid sequence of SEQ ID NO:2, where claim 60 does not even require both the nonapeptide region of claim 45 and the intervening, carboxyl-terminal, region of the sentrin-specific protease having the amino acid sequence set forth in SEQ ID NO:2.

The specification fails to describe the design or preparation of generic, functional, sentrin-specific proteasse of claims 45-50 and 55-60 comprising even the 200 carboxyl-terminal amino acids of SEQ ID NO:2, yet differing elsewhere in their amino acid sequence, particularly where the specification admits in Example 4, at pages 85-86, that

although the integral sentrin-specific protease of SEQ ID NO:2 cleaves sentrin-1 and sentrin-2 from many polypeptides, it cannot cleave sentrin-1 from sentrinized RanGAP1. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. §112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The specification furnishes no relevant identifying characteristics of a generic sentrin-specific protease comprising no particular region of 200 amino acids that also comprises the nonapeptide of claim 45, but lacks the rest of SEQ ID NO:2. Nothing demonstrates that, at the time the specification was filed, Applicant was "able to envision" enough of the structure of any of these undisclosed generic SENP1 polypeptides to provide the public with identifying "characteristics [that] sufficiently distinguish [them] . . . from other materials". *Fiers*, 25 USPQ2d at 1604 (citing *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). The specification's treatment of the claimed subject matter is considered to be entirely prospective where skilled artisans in the relevant field of molecular biology could not predict the structure or other properties of claimed products.

Claims 45-50 and 55-60 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for the preparation of a sentrin-specific protease comprising an amino acid sequence that comprises the carboxyl-terminal 200 amino acids of SEQ ID NO:2 and that is encoded by a polynucleotide that hybridizes to the nucleic acid sequence of SEQ ID NO:1 from position 157 through position 2085, inclusive, in 0.10M NaCl at 70°C,

does not reasonably provide enablement for a nucleic acid sequence encoding a generic de-sentrinase comprising as much as any 200 amino acids of a portion of the amino acid sequence of SEQ ID NO:2 yet diverges elsewhere from SEQ ID NO:2 by amino acid substitutions, deletions and insertions, or combinations thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The above limitation statement incorporates limitations (1) found in the sequence disclosure, where the codons specifying the methionines at positions 1, 8, 10, and 633

of SEQ ID NO:2, as well as the termination codon "tga" following the codon specifying leucine at position 643 of SEQ ID NO:2, can be identified, (2) at page 10, lines 14 and 15, of the specification, and (3) in the current claims 50 and 60. Claims 45-50 and 55-60 are rejected because they contemplate the preparation of sentrin-specific proteases comprising arbitrary assignments of amino acid substitutions, additions or deletions in larger or smaller portions of SEQ ID NO:2 where the largest portion of any rejected claim comprises but 31% of the amino acid sequence of SEQ ID NO:2. There is no teaching in the specification that describes where, and how, the amino acid sequence of SEQ ID NO:2 might be altered, yet provide a protease with the disclosed utility, the ability to cleave sentrin-1 and sentrin-2 from many sentrinized polypeptides. Indeed, neither the prior art made of record herewith taken together with the specification can identify any particular amino acids in the primary sequence of the native SENP1 amino acid sequence set forth in SEQ ID NO:2 that might be altered, nor teach the nature of any alterations that may be made, which would permit resulting polypeptides to function as sentrin-specific proteases. The prior art made of record herewith does not show that the state of the relevant art of molecular biology, combined with the disclosure of the instant specification, will support such extensive alteration. Mere sequence perturbation will not enable the design and preparation of nucleotide sequences encoding a myriad of divergent proteases and provide the public with a nucleotide sequence encoding a de-sentrinase that retains its useful function.

It is well settled that 35 U.S.C. §112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed.

Cir. 1988) (discussing eight factors relevant to analysis of enablement). Applying the factors discussed in *Wands* to Applicant's disclosure, it is apparent that:

a) the specification lacks adequate, specific, guidance for altering the amino acid sequence of SEQ ID NO:2 to the extent permitted by the claims,

b) the specification lacks working examples wherein the amino acid sequence of SEQ ID NO:2 is altered in any way,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such alteration, and,

d) unpredictability exists in the art where no de-sentrinases represented by the amino acid sequence of the disclosed SENP1 have had any amino acid positions specifically identified for concurrent modification.

Thus the scope of the claimed subject matter embraced by claims 45-50 and 55-60 is unsupported by the present specification, even when taken in combination with the teachings available in the prior art. Limitation of the subject matters as indicated in the limitation statement hereinabove is required in order to overcome this rejection and will also overcome the rejections above for lack of adequate written description as well as the following rejections under 35 U.S.C. § 102.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 55-58 are rejected under 35 U.S.C. §102(b) as being anticipated by the human cDNA clone "IMAGE:684275" having the GenBank accession No. AA236084 published electronically in 1997 by the Cancer Genome Anatomy Project of the National Cancer Institute, made of record herewith.

In view of the lack of any requirement for a structure that permits the function of a "sentrin-specific protease SENP1" of claims 55-58, the 345-nucleotide sequence of the EST having Accession No. AA236084, which is identical to the nucleic sequence of SEQ ID NO:1 from position 796 through position 1140, inclusive, and encodes a 114-amino acid region, of the amino sequence of SEQ ID NO:2 from position 214 through

position 328, inclusive, is inherently considered to disclose the subject matter of claims 55-58.

Claims 55-58 are rejected under 35 U.S.C. §102(b) as being anticipated by the 3' region of the human cDNA clone "IMAGE:684275" with GenBank accession No. AA236014 published in 1997 by the Cancer Genome Anatomy Project of the National Cancer Institute, made of record with Applicant's Information Disclosure.

In view of the lack of any requirement for a structure that permits the function of a "sentrin-specific protease SENP1" of claims 55-58, the 382-nucleotide sequence of the EST having Accession No. AA236014, which is identical in sequence to the nucleic sequence of SEQ ID NO:1 from position 995 through position 1376, inclusive, and encodes a region of the amino sequence of SEQ ID NO:2 from position 280 through position 407, inclusive, is inherently considered to disclose the subject matter of claims 55-58.

Claims 55-57 are rejected under 35 U.S.C. §102(b) as being anticipated by the human cDNA clone of Adams et al. designated EST33924 and having the GenBank accession No. AA330056 published electronically in 1997 by the Institute of Genomic Research, made of record herewith.

In view of the lack of any requirement for a structure that permits the function of a "sentrin-specific protease SENP1" of claims 55-55, the 274 nucleotides of the nucleic acid sequence of the EST having Accession No. AA330056, which is identical in sequence to the nucleic sequence of SEQ ID NO:1 from position 1290 through position 1563, inclusive, and encodes a region of the amino sequence of SEQ ID NO:2 from position 379 through position 469, inclusive, is inherently considered to disclose the subject matter of claims 55-57.

Allowable Subject Matter

Claim 54 is, in part, allowable but objected to because it reads on non-elected subject matter and claim 63 is allowed herewith. Although the three extensive prior art EST nucleotide sequence disclosures cited above overlap and comprise 768 contiguous nucleotides of SEQ ID NO:1 and encoding 256 amino acids of SEQ ID NO:2, there is no

indication that they may be combined to form a nucleic acid sequence encoding a sentrin-specific protease having the amino acid sequence of SEQ ID NO:2. The yeast Ulp1 protease of Li et al., 1999, made of record with Applicant's Information Disclosure, is the only prior art polypeptide having a similar function but its amino acid sequence has too little similarity to SEQ ID NO:2 to guide the assembly of the EST coding regions or determine the rest of the amino acid sequence of a sentrin-specific protease of SEQ ID NO:2.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

William W. Moore
18 September 2006

NASHAAT T. NASHED PHD.
PRIMARY EXAMINER